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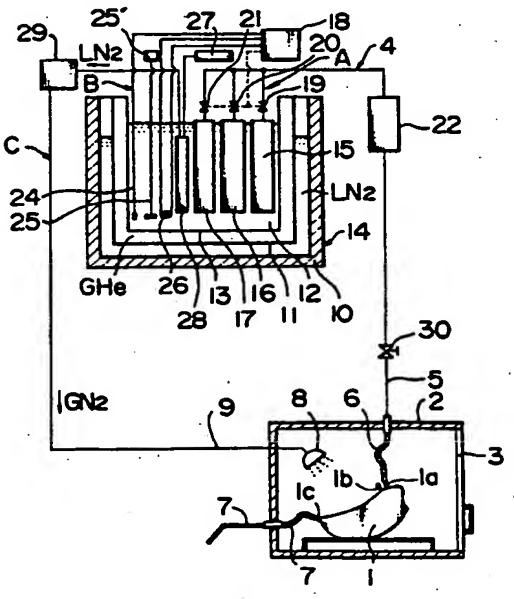
(54) Method of preserving organ and apparatus for preserving the same.

(57) A method of preserving an organ which comprises first perfusing step of injecting blood uniformly perfusing choline from an artery or portal vein of the excised organ while gradually lowering its temperature and exhausting it from the vein continuing until the liquid is lowered to the first proximity lowering temperature before its solidifying temperature, second perfusing step of perfusing refrigerating defect preventing dimethyl sulfoxide or glycerin instead of the blood uniformly perfusing liquid while gradually lowering its temperature from the first proximity lowering temperature continuing until the agent becomes the second proximity lowering temperature before its solidifying temperature, third perfusing step of perfusing the final perfusing liquid of low solidifying temperature lower than alcohol or ether instead of the agent while gradually lowering the liquid form the second proximity lowering temperature continuing until the liquid becomes the third proximity lowering temperature before its solidifying temperature, or until the liquid is frozen.



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as to prolong the preserving period of time, but when the organ is frozen according to the conventional method, a cell necrocytosis occurs, causing the organ itself to occur a meronecrosis.

Accordingly, a primary object of this invention is to provide a method of preserving an organ which can freeze the organ without occurring a cell necrocytosis and can semipermanently preserve the cell as well as which can thaw the frozen organ in case of transplanting the organ.

Another object of this invention is to provide an apparatus for preserving and thawing the frozen organ. The above and other relates objects and features of the invention will be apparent from a reading of the following description of the disclosure found in the accompanying drawings and the novelty thereof pointed out in the appended claims.

Fig. 1 is a partial longitudinal sectional view of one preferred embodiment of an apparatus for preserving an organ to executing a method of preserving the organ according to the present invention for the explanatory purpose; and

Fig. 2 is a schematic view of the essential part of another preferred embodiment of the apparatus according to the present invention for the explanatory purpose.

provided at outflow pipes of the containers 15, 16 and 17 are suitably opened or closed under the control of a controller 18, and the choline, DMSO and alcohol are selectively supplied to the artery 1a or portal vein 1b of the organ 1 by the operation of a pump 22 provided at the pipe 5.

On the other hand, in a liquid supplying mechanism A which is schematically shown in Fig. 2, first, second and third containers 15, 16 and 17 are provided externally of the cooling tank 14, and a heat exchanger 23 formed between the first, second and third control valves 19, 20 and 21 and the pump 22 is dipped in the refrigerant 12 of the cooling tank 14.

In the tank 14 is provided a refrigerant temperature controlling mechanism B which can control the temperature of the refrigerant 12. In the embodiment exemplified in Fig. 1, a temperature sensor 24, an agitator 25 and an electric heater 26 are dipped in the refrigerant 12 in the mechanism B. The sensor 24 and the heater 26 are connected to the controller 18. Reference numeral 25' designates a motor for driving the agitator 25.

Further, in the tank 14 is provided an organ temperature controlling mechanism C. The LN_2 is supplied from an organ refrigerant bomb 27 which contains liquid nitrogen to a gas supplying container 28 which is disposed in the refrigerant

The above lowering temperature is controlled by controlling as described above the refrigerant 12 cooled through the GHe in the tank 11 from the LN_2 in the tank 10 by the mechanism B. Since the solidifying temperature of the choline is approx. 0°C, the first perfusing step may control the lowering temperature so that the first proximity lowering temperature becomes approx. 1 to 2°C. In order to lower, for example, the blood uniform perfusing liquid from the body temperature of 37°C to 2°C, the temperature lowering speed is 3.5°C/min, and the perfusing time can be set to approx. 10 min.

The GN_2 controlled at its temperature is injected from the nozzle 8 by operating the heat exchanger 29, thereby rapidly equalizing the atmospheric temperature in the container 2 to the temperature of the blood uniformly perfusing liquid to be lowered at its temperature to eliminate the temperature gradient between the inner and the outer temperatures of the organ 1. This is also continued in the following steps.

Then, the method is transferred to the second perfusing step of supplying and perfusing a freezing defect preventing agent such as dimethyl sulfoxide or glycerin in the container 16 to the organ 1 instead of the blood uniformly perfusing liquid by controlling to close the valve 19 and to open the valve 20 instead of

the third proximity temperature before its solidifying temperature or until the perfusing liquid is frozen to stop perfusing. In case of the alcohol, since the solidifying temperature is approx. -80°C, the third proximity lowering temperature may, for example, be set to -60°C or -80°C.

In fact, in this third step, it takes approx. 30 min of perfusing period of time at the lowering speed of 0.1°C/min. to lower the alcohol from -4°C to -37°C, and it further takes approx. 5 min of perfusing period of time at the lowering temperature of 5°C/min. under the lowering condition from -37°C to -60°C.

The frozen organ obtained through the first to third steps as described above is then preserved in the frozen state. In case of the above embodiment, the frozen organ may be preserved in a refrigerator which is maintained at approx. -80°C or may be preserved in liquefied gas such as liquefied nitrogen.

The frozen organ thus preserved is then thawed for transplanting it. The thawing means can be performed substantially reversely by the steps of freezing the organ.

More particularly, the frozen organ is removed from the preserved position, and is set to the state shown in Fig. 1. In this case, the atmospheric temperature in the

transplantation by applying the predetermined blood to the organ.

According to the first method of the present invention as described above, the choline is not merely perfused in the organ instead of the blood as the conventional method and the organ is preserved at approx. 4°C, but the blood uniformly perfusing liquid such as choline is gradually lowered at its temperature in the first perfusing step until the liquid is perfused to the first proximity lowering temperature before its solidifying temperature. Accordingly, the organ is not affected by the influence of the abrupt temperature change, but the nutriments equivalent to the blood are supplied to the organ when the metabolism of the cells of the organ is most active at 1 to 2°C.

In the second thawing step, the refrigerating defect preventing agent is further lowered at its temperature and is lowered to the second proximity lowering temperature before the solidifying temperature of the agent. Accordingly, the moisture content in the cells is absorbed due to the osmotic pressure difference from the moisture content in the cells or the organ and the agent in this step as described above. Consequently, when the organ is frozen by the temperature fall in the next step, no moisture is contained, and the organ can be frozen

defect preventing agent is gradually raised from the above second proximity lowering temperature instead of the final perfusing liquid, and is continued until becoming the first proximity lowering temperature, and further the blood uniformly perfusing liquid is gradually raised at its temperature from the first proximity lowering temperature instead of the agent, and is continued until becoming the body temperature in the third thawing and perfusing step of perfusing the liquid, and the predetermined blood is applied to the organ. Therefore, the frozen organ can be readily thawed without any damage.

Further, in the third embodiment of the present invention, the apparatus for preserving the frozen organ, which comprises the perfusing and thawing unit 4, and the heat insulating container 2 capable of containing the organ 1, the unit 4 having a refrigerant tank 14 containing the refrigerant 12 such as Freon and thermally insulated, the refrigerant temperature controlling mechanism B capable of controlling the temperature of the refrigerant 12 by the controller 12, the gas supplying container 28 supplied with the refrigerant from the organ refrigerant bomb 27 dipped in the refrigerant 12 for the tank 14, the container 28 having the organ temperature controlling mechanism C connected through the heat exchanger 21 to the gas supply pipe, and the liquid supplying mechanism A for selectively

WHAT IS CLAIMED IS:

1. A method of preserving an organ comprising:

first perfusing step of injecting blood uniformly perfusing liquid such as choline from an artery or portal vein of the excised organ while gradually lowering its temperature and exhausting it from the vein, continuing said step until the liquid is lowered to the first proximity lowering temperature before its solidifying temperature,

second perfusing step of perfusing refrigerating defect preventing agent such as dimethyl sulfoxide or glycerin instead of the blood uniformly perfusing liquid while gradually lowering its temperature from the first proximity lowering temperature, continuing said second step until the agent becomes the second proximity lowering temperature before its solidifying temperature,

third perfusing step of perfusing the final perfusing liquid of low solidifying temperature lower than the agent such as alcohol or ether instead of the agent while gradually lowering the liquid from the second proximity lowering temperature, continuing said third step until the liquid becomes the third proximity lowering temperature before its solidifying temperature, or until the liquid is frozen, and

preserving the frozen organ thus obtained in the frozen

state,

the first thawing and perfusing step of thawing the final perfusing liquid in the blood vessel of said organ by gradually raising the organ thus preserved and frozen and then perfusing the liquid from said artery or portal vein to the vein while gradually raising the liquid, continuing said first thawing and perfusing step until becoming said second proximity lowering temperature,

the second thawing and perfusing step of perfusing the agent instead of the liquid while gradually raising the temperature from said second proximity lowering temperature, continuing said second thawing the perfusing step until becoming said first proximity lowering temperature,

the third thawing and perfusing step of perfusing the blood uniformly perfusing liquid instead of the agent while gradually raising the liquid from said first proximity lowering temperature, continuing said third thawing and perfusing step, and

applying predetermined blood to said organ.

3. An apparatus for preserving a frozen organ comprising:

a perfusing and thawing unit, and

a heat insulating container capable of containing said organ,

said unit having a refrigerant tank containing the refrigerant such as Freon and thermally insulated,

refrigerant temperature controlling mechanism comprises a temperature sensor connected to said controller, an electric heater, and an agitator.

5. The apparatus as claimed in claim 1, wherein the first, second and third containers of said liquid supplying mechanism are dipped in the refrigerant in said cooling tank, and the opening or closing of said first, second and third control valves provided at said respective container are controlled by said controller.

6. The apparatus as claimed in claim 1, wherein the heat exchanger formed between the first, second and third control valves of said liquid supplying mechanism and the pump is dipped in the refrigerant in said cooling tank.

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FIG. 1

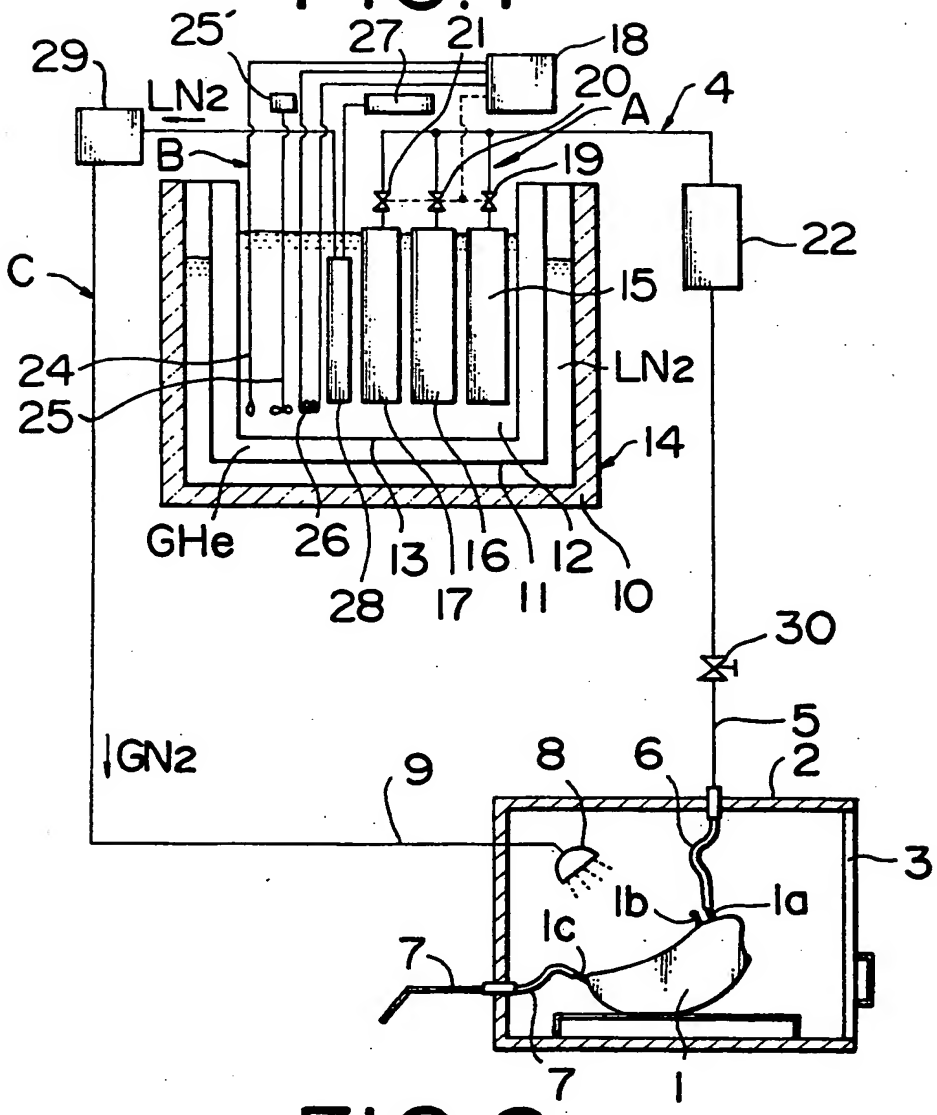
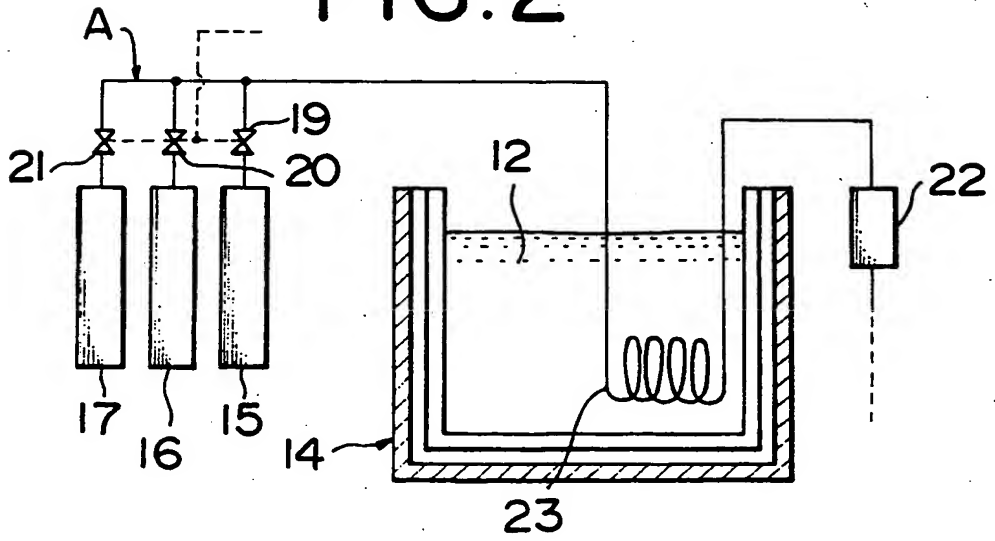


FIG. 2



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EUROPEAN SEARCH REPORT

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Application number

EP 83 30 3133

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. ³)
A	KOELTECHNIEK, vol. 67, no. 7, July 1974, pages 91-100, Nederlandse Vereniging voor Koeltechniek, Apeldoorn, NL. A.U. SMITH: "Twenty five years of research in low temperature" * Page 99 *	1	A 01 N 1/02
A	FR-A-2 077 641 (L'AIR LIQUIDE)	3-6	
A	FR-A-2 151 092 (R. DOERIG)	3-6	
A	DE-A-1 938 275 (BAXTER)	3-6	
A	GB-A-1 422 356 (VICKERS)		

TECHNICAL FIELDS SEARCHED (Int. Cl. ³)

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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	23-09-1983	PELTRE CHR.

CATEGORY OF CITED DOCUMENTS

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